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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/560,476	12/12/2005	Frans Eduard Janssens	PRD2076f-PCT-USA	3183

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PHILIP S. JOHNSON
JOHNSON & JOHNSON
ONE JOHNSON & JOHNSON PLAZA
NEW BRUNSWICK, NJ 08933-7003

EXAMINER	
JAVANMARD, SAHAR	

ART UNIT	PAPER NUMBER
1617	

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Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/560,476	JANSSENS ET AL.	
	Examiner	Art Unit	
	SAHAR JAVANMARD	1617	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *11 June 2008*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-17* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-17* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☒ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Status of the Claims

This Office Action is in response to Applicant's Restriction Requirement remarks filed on June 11, 2008. Claim(s) 1-17 are pending. Applicant's election of Group I drawn to a pharmaceutical composition and election of species of {4-[4-(1-Benzoyl-piperidin-4-yl)-piperazin- 1-yl]-2-benzyl-piperidin- 1-yl}-(3,5-bis-trifluoromethyl-phenyl)-methanone (compound of formula I), and morphine (opioid analgesic) with traverse of the restriction requirement in the reply is acknowledged.

The traversal is on the grounds that Groups I-III do not relate to a single inventive concept under PCT Rule 13.2 because they lack the same or corresponding technical feature. Upon further consideration, the arguments were found persuasive and the restriction requirement is hereby removed. Claim(s) 1-17 are examined herein insofar as they read on the elected invention.

For sake of compact prosecution, the "use" claims have been interpreted as method claims.

Double Patenting

The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees. A nonstatutory obviousness-type double patenting rejection is appropriate where the conflicting claims are not identical, but at least one examined application claim is not patentably distinct from the reference claim(s) because the examined application claim is either anticipated by, or

would have been obvious over, the reference claim(s). See, e.g., In re Berg, 140 F.3d 1428, 46 USPQ2d 1226 (Fed. Cir. 1998); In re Goodman, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); In re Longi, 759 F.2d 887,225 USPQ 645 (Fed. Cir. 1985); In re Van Omum, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); In re Vogel, 422 F.2d 438, 164 USPQ 619 (CCPA 1970); and In re Thorington, 418 F.2d 528, 163 USPQ 644 (CCPA 1969).
A timely filed terminal disclaimer in compliance with 37 CFR 1.321 (c) or 1.321(d) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the conflicting application or patent either is Shown to be commonly owned with this application, or claims an invention made as a result of activities undertaken within the scope of a joint research agreement.
Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

Claims 1-6 and 8-11 are rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims 6 and 7 of U.S. Patent No. 7,410,970 B2 to Janssens et al. Although the conflicting claims are not identical, they are not patentably distinct from each other because the instant claims are directed to a pharmaceutical composition comprising a compound of formula I and an opioid analgesic. Although U.S. Patent No. 7,410,970 does not specifically claim an opioid analgesic, it claims a pharmaceutical composition *comprising* a compound of formula I, the "comprising" language leaves the composition open to other components, therefore the composition could also contain an opioid analgesic.

Claims 1-6 and 8-11 are provisionally rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claim 11-13 of copending Application No. 10/540,045. Although the conflicting claims are not identical, they are not patentably distinct from each other because the instant claims are directed

to a pharmaceutical composition comprising a compound of formula I and an opioid analgesic. Although Application '045 does not specifically claim an opioid analgesic, it claims a pharmaceutical composition *comprising* a compound of formula I, the "comprising" language leaves the composition open to other components, therefore the composition could also contain an opioid analgesic. Further, both Applications claim the administration of a compound of formula I for the treatment of pain.

This is a provisional obviousness-type double patenting rejection because the conflicting claims have not in fact been patented.

Claim Rejections - 35 USC § 112-1st

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 1-17 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while enabling for compounds of formula I wherein n=1, m=1, and p=1 and R2 is 3,5-bis-trifluoromethyl-phenyl, does not reasonably provide enablement for compounds of formula I wherein n=0,1 or 2; m= 1 or 2; and p=1 or 2 and R2 is selected from the group consisting of those as set forth in the instant claims. The specification does not provide evidence that Applicant is in possession of all the compounds of formula I wherein n=0, 1 or 2; m= 1 or 2; and p=1 or 2 and R^2 is selected from the group consisting of alkyl, Ar^2, Ar^2-alkyl, Het^1 or Het^1-alkyl. Thus, the various

combinations of n, m and p are very broad when they are not limited to one and R^2 limited to 3,5-bis-trifluoromethyl-phenyl as cited in claims 1-17.

The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to practice the invention commensurate in scope with these claims. The specification does not provide evidence that Applicant is in possession of all the compounds of formula I wherein n=0, 1 or 2; m= 1 or 2; and p=1 or 2 and R^2 is selected from the group consisting of alkyl, Ar^2, Ar^2-alkyl, Het^1 or Het^1-alkyl.

The instant specification fails to provide information that would allow the skilled artisan to practice the instant invention without undue experimentation. Attention is directed to *In re Wands*, 8 USPQ2d 1400 (CAFC 1988) at 1404 where the court set forth the eight factors to consider when assessing if a disclosure would have required undue experimentation. Citing *Ex parte Forman*, 230 USPQ 546 (BdApls 1986) at 547 the court recited eight factors:

(1) the nature of the invention; (2) the state of the prior art; (3) the relative skill of those in the art; (4) the predictability or unpredictability of the art; (5) the breadth of the claims; (6) the amount of direction or guidance presented; (7) the presence or absence of working examples; and (8) the quantity of experimentation necessary.

(1). The Nature of the Invention:

All of the rejected claims are drawn to an invention which pertains to a

pharmaceutical composition comprising compounds of formula I and an opioid analgesic as described in claims 1-17.

The nature of the invention is complex in that it encompasses a numerous number of compounds with varying core structures.

(2). Breadth of the Claims:

The complex nature of the subject matter of this invention is greatly exacerbated by the breadth of the claims. The claims encompass a numerous number of compounds with varying core structures. There are countless possible compounds encompassed by compounds of formula I. The claims are therefore much broader than the enabling disclosure.

(3). Guidance of the Specification:

The guidance given by the specification is limited to a core structure wherein n=m=p=1 and R^2=3,5-bis-trifluoromethyl-phenyl.

(4). Working Examples:

Applicant provides examples of compounds of formula I and compositions thereof wherein n=m=p=1 R^2=3,5-bis-trifluoromethyl-phenyl as shown in table I in the specification.

(5). State of the Art:

The composition of compounds of formula I with an opioid analgesic are considered novel, however Applicant has not provided sufficient evidence to indicate that all the compounds of formula I wherein n=0, 1 or 2; m= 1 or 2; p=1 or 2 and R^2 is selected from the group consisting of alkyl, Ar^2, Ar^2-alkyl, Het^1 or Het^1-alkyl are in possession.

(6). Nature and predictability of the invention

The nature of the invention is directed towards medicine and is therefore physiological in nature. It is well established that "the scope of enablement varies inversely with the degree of unpredictability of the factors involved," and physiological activity is generally considered to be an unpredictable factor. See *In re Fisher*, 427 F.2d 833, 839, 166 USPQ 18, 24 (CCPA 1970).

(7). The Quantity of Experimentation Necessary:

Considering the state of the art as discussed above, particularly with regards to claim 1 and the lack of guidance provided in the specification, one of ordinary skill in the art would be burdened with undue experimentation to practice the invention commensurate in the scope of the claims.

Genetech, 108 F.3d at 1366 states that "a patent is not a hunting license. It is not a reward for search, but compensation for its successful conclusion" and "[p]atent protection is granted in return for an enabling disclosure of an invention, not for vague intimations of general ideas that may or may not be workable."

Therefore, all the compounds of formula I wherein n=0, 1 or 2; m= 1 or 2; and p=1 or 2 and R^2 is selected from the group consisting of alkyl, Ar^2, Ar^2-alkyl, Het^1 or Het^1-alkyl of the claims is not considered to be enabled by the instant specification.

Claim Rejections - 35 USC § 112-1st

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 12-16 are rejected under 35 U.S.C. 112, first paragraph, for scope of enablement because the specification, while being enabling for the treatment of pain, does not reasonably provide enablement for the prevention of pain as recited in these claims.

The instant claims are drawn to a pharmaceutical composition and a method for the prevention of pain. The instant specification fails to provide information that would allow the skilled artisan to practice the instant invention. Attention is directed to *In re Wands*, 8 USPQ2d 1400 (CAFC 1988) at 1404 where the court set forth the eight factors to consider when assessing if a disclosure would have required undue experimentation. Citing *Ex parte Forman*, 230 USPQ 546 (BdApls 1986) at 547 the court recited eight factors:

(1) the nature of the invention; (2) the state of the prior art; (3) the relative skill of those in the art; (4) the predictability or unpredictability of the art; (5) the breadth of the claims;

(6) the amount of direction or guidance presented; (7) the presence or absence of working examples; and (8) the quantity of experimentation necessary.

Nature of the invention:

The instant invention pertains to a method for the prevention of pain.

The state of the prior art:

The skilled artisan would view that the prevention of one or more symptoms of pain totally, absolutely, or permanently, is highly unlikely, since one cannot guarantee that the pain will always be prevented.

The relative skill of those in the art:

The relative skill of those in the art is very high.

The predictability or lack thereof in the art:

The skilled artisan would view that the treatment to prevent pain, absolutely, or permanently is highly unpredictable.

The amount of direction or guidance presented and the presence or absence of working examples:

In the instant case, no working examples are presented in the specification as filed showing how to prevent pain totally, absolutely, or permanently. Note that lack of a

working example, is a critical factor to be considered, especially in a case involving an unpredictable and undeveloped art. See MPEP 2164.

Genentech, Inc. v. Novo Nordisk, 108 F.3d at 1366, states that "a patent is not a hunting license. It is not a reward for search, but compensation for its successful conclusion" and "[p]atent protection is granted in return for an enabling disclosure of an invention, not for vague intimations of general ideas that may or may not be workable".

Therefore, in view of the *Wands* factors, e.g., the amount of direction or guidance provided, absence of working examples, and the predictability of the art discussed above, to practice the claimed invention herein, a person of skill in the art would have to engage in undue experimentation to test the combination in the instant claims whether preventing pain totally, absolutely, or permanently.

Claim Rejections - 35 USC § 112-2nd

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 1-17 are rejected under 3 5 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claim 1 sets forth the notation of R^1 and R_1. It is not clear whether these are intended to be the same variable or different.

Claim 6 refers to the compounds by number rather than by structure.

As per claims 16 and 17, the recitation, "prodrugs thereof" renders claims indefinite. The recitation, "prodrugs thereof" is not clearly defined in the specification. Hence, one of ordinary skill in the art could not ascertain and interpret the metes and bounds of the patent protection desired as to "prodrugs thereof" of compounds herein, since one of ordinary skill in the art would clearly recognize that many various groups could possibly substituting these compounds. As a result, any significant structural variation to a compound would be reasonably expected to alter its properties, e.g., physical, chemical, physiological effects and functions. Thus, it is unclear as to what "prodrugs thereof" of compounds herein would be encompassed thereby.

As per claim 17, states "...for reducing and/or overcoming the tolerance..." It is not clear to one of ordinary skill in the art to ascertain and interpret the metes and bounds of the patent protection desired. What is the measure by which one can determine if in fact tolerance has been reduced and/or overcome?

Claims 12-17 provides for the use of a pharmaceutical composition, but, since the claim does not set forth any steps involved in the method/process, it is unclear what method/process applicant is intending to encompass. A claim is indefinite where it merely recites a use without any active, positive steps delimiting how this use is actually practiced.

For sake of compact prosecution, the "use" claims have been interpreted as method claims.

Claim Rejections - 35 USC § 101

35 U.S.C. 101 reads as follows:

> Whoever invents or discovers any new and useful process, machine, manufacture, or composition of matter, or any new and useful improvement thereof, may obtain a patent therefor, subject to the conditions and requirements of this title.

Claims 12-17 are rejected under 35 U.S.C. 101 because the claimed recitation of a use, without setting forth any steps involved in the process, results in an improper definition of a process, i.e., results in a claim which is not a proper process claim under 35 U.S.C. 101. See for example *Ex parte Dunki*, 153 USPQ 678 (Bd.App. 1967) and *Clinical Products, Ltd.* v. *Brenner*, 255 F. Supp. 131, 149 USPQ 475 (D.D.C. 1966).

Conclusion

Claims 1-17 are not allowed.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Sahar Javanmard whose telephone number is (571) 270-3280. The examiner can normally be reached on 8 AM-5 PM MON-FRI (EST).

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Sreeni Padmanabhan can be reached on (571) 272-0629. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

/S. J./

Examiner, Art Unit 1617

/SREENI PADMANABHAN/

Supervisory Patent Examiner, Art Unit 1617